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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,428	12/06/2006	Jose Francisco Aguirre	7572-73329-01	6576

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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,428	AGUIRRE ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19-22 and 24-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10,12-17,19-22 and 24-32* is/are rejected.

7)☒ Claim(s) *7,8 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/9/07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 10-22, 30-32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Parent claim 1 is drawn to a chimeric empty capsid comprising two different types of proteins. The nucleic acid of claim 10 is not a further limitation of the chimeric capsid of claim 1. This affects the dependent claims. In the interest of compact prosecution, claim 10 has been treated as if it were an independent claim drawn to a nucleotide sequence encoding a fusion of IBDV VP3 and a heterologous peptide. However, this treatment does not relieve applicant of the burden of response to this objection.

Specification

The disclosure is objected to because of the following informalities: it contains at least one sequence recitation that is not accompanied by the required SEQ ID number. See page 30, line 6.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition, does not reasonably provide enablement for vaccines against infectious agents other than IBDV or enablement for gene therapy vectors. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There are two separate issues here, concerning vaccines and concerning gene therapy.

Regarding vaccines, the specification and the prior art teach that VP3 is found on the interior and VP2 is found on the exterior of VP2/VP3 particles, and that a fusion to the C terminus of VP3 extends into the center of the particle. The specification provides evidence that a small peptide can be fused to the N terminus of VP3 without disrupting assembly, and the prior art teaches that a large peptide can be fused to the C terminus without disrupting assembly. However, neither of these fusions would be likely to expose the heterologous sequence on the surface of the particle. Therefore, one would have reason to believe that the immune response directed against the heterologous sequence would be less robust than an immune response directed against a surface-exposed sequence. The specification provides evidence that the N-terminal fusion can prime an immune reaction on pages 29-31. However, there is no evidence that the products can induce an immune response that is sufficient to protect against disease, as required for a vaccine. Therefore, considering the unpredictability of the art, the limited teachings in the specification, and the absence of working examples, it is concluded that undue experimentation would be required to enable vaccines against infectious agents other than IBDV itself.

In regard to gene therapy, the specification does not teach how to package a heterologous gene sequence into the claimed chimeric empty capsids, or how to obtain successful therapeutic expression of the packaged sequence. It is also noted that IBDV

host range is limited to birds, and the state of the art of gene therapy in birds is even less advanced than the less-than-routine state of the art in mammals. Furthermore, there is no evidence that the claimed empty capsids can be effectively taken up by host cells, since they do not contain all of the native virion proteins. Considering the limited teachings in the specification, the state of the art of avian gene therapy, and the absence of working examples, it is concluded that undue experimentation would be required to make and use the claimed gene therapy vector.

Claims 20-22, 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making chimeric empty capsids by co-expressing VP2 and VP3 fusion protein, does not reasonably provide enablement for a method of making capsids by expressing the VP3 fusion protein alone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The specification, throughout, requires expression of both VP2 and VP3 to make IBDV virus-like particles. However, these claims require only a sequence encoding the VP3 fusion protein. Considering the absence of guidance in the specification, it is concluded that undue experimentation would be required to enable the invention as now claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 6, 9, 10, 13-17, 19-21, 24- 29, 31, 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Chevalier et al (Journal of Virology 76:2384-2392, 2002) (cited in IDS). Chevalier teaches recombinant production of IBDV capsid-like particles comprising VP2 and a VP3-linker-GFP fusion protein. See figure 4. Chevalier therefore clearly anticipates claims 1, 2, 4, 6, 9, 10, 13-17, 19-21, 31, and 32. Claims 24-29 are drawn to products comprising a single component, the chimeric empty capsid of claim 1. Since the reference teaches the chimeric empty capsid of claim 1, the reference meets the limitations of those claims as well, even though the reference does not teach the intended use recited in the claims.

Claims 10, 11, 13, 15-17, 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kochan et al (Arch. Virol. 148:723-744, 2003) (cited in IDS). Kochan teaches a VP3 with an N-terminal histidine tag, and expression systems and host cells for expressing the protein, thereby meeting all the limitations of these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chevalier et al (Journal of Virology 76:2384-2392, 2002) as applied to claims 1, 2, 4, 6, 9, 10, 12-17, 19-21, 24- 29, 31, 32 above, and further in view of Ulrich et al (Intervirology 39(1):126-132, 1996). Claim 3 differs from Chevalier in that it requires a fusion with a polypeptide useful in vaccination, therapy, or diagnosis, unlike the green fluorescent protein (GFP) used by Chevalier. However, Ulrich teaches many different types of chimeric virus-like particles made with proteins of vaccine interest. Therefore, substitution of an immunogenic protein for the GFP of Chevalier is seen as an obvious variation. In addition, claim 5 requires two or more polypeptides. Ulrich also teaches VLPs with multiple foreign peptides, see for example the second full paragraph of page 128, second column. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chevalier et al (Journal of Virology 76:2384-2392, 2002) as applied to claims 1, 2, 4, 6, 9, 10, 12-17, 19-21, 24- 29, 31, 32 above, and further in view of Azad et al (US 5614409). Claim 22 differs from Chevalier in requiring a yeast host cell, while Chevalier

used an insect host cell for recombinant production of the IBDV VLPs. However, Azad teaches yeast as a host cell for producing IBDV proteins. Although Azad did not observe assembly of VLPs, Chevalier teaches modification of VP3 as essential for efficient assembly of VLPs. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in assembling VLPs in other hosts, such as yeast, using a modified protein as taught by Chevalier. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chevalier et al (Journal of Virology 76:2384-2392, 2002) as applied to claims 1, 2, 4, 6, 9, 10, 12-17, 19-21, 24- 29, 31, 32 above, and further in view of Oña et al (Virology 322:135-142, 2004) (cited in IDS). Claim 30 differs from the above in requiring separate gene constructs for the expression of pVP2 and the VP3 fusion protein. Oña teaches that coexpression of pVP2 and VP3 from separate genes results in successful assembly of virus-like particles. Therefore, modification of the teachings of Chevalier by separating the two coding sequences into two separate constructs for coexpression is seen as an obvious variation, absent unexpected results. Please note, applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Allowable Subject Matter

Claims 7, 8, and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: The prior art does not teach or particularly suggest successful assembly of VLPs with a heterologous sequence fused to the N-terminus of VP3. Chevalier et al (Journal of Virology 76:2384-2392, 2002) teaches that assembly of VP2/VP3 VLPs is very sensitive to the C-terminal sequence of VP3, in that assembly only occurs if the C-terminus is altered. Tacken et al (Virology 312:306-319, 2003) teaches that the N-terminal sequence is involved in VP3/VP3 association, therefore the effect of an N-terminal fusion on VLP assembly would have been unpredictable.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on varying dates and times; please leave a message.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
Primary Examiner, Art Unit 1648

1/7/09